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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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10/521,354

10/20/2005

Martin Quibell

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29933 7590 08/28/2008  
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EXAMINER

HAVLIN, ROBERT H

ART UNIT

PAPER NUMBER

1626

MAIL DATE

DELIVERY MODE

08/28/2008

PAPER

**Please find below and/or attached an Office communication concerning this application or proceeding.**

The time period for reply, if any, is set in the attached communication.

<b>Office Action Summary</b>	<b>Application No.</b> 10/521,354	<b>Applicant(s)</b> QUIBELL ET AL.	
	<b>Examiner</b> Robert Havlin	<b>Art Unit</b> 1626	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

### Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

### Status

- 1) ☒ Responsive to communication(s) filed on 02 July 2008.
- 2a) ☐ This action is **FINAL**.                      2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

### Disposition of Claims

- 4) ☒ Claim(s) 1-31,33,35,37-39,41,43-45,47,49-52,58 and 60-74 is/are pending in the application.
- 4a) Of the above claim(s) 9-12,29,33,35,37-39,41,43-45,47,50,52 and 60-72 is/are withdrawn from consideration.
- 5) ☐ Claim(s) \_\_\_\_\_ is/are allowed.
- 6) ☒ Claim(s) 1-8,13-28,30,31,49,51,58,73 and 74 is/are rejected.
- 7) ☒ Claim(s) 1-8,13-28,30,31,49,51,58,73 and 74 is/are objected to.
- 8) ☐ Claim(s) \_\_\_\_\_ are subject to restriction and/or election requirement.

### Application Papers

- 9) ☒ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on \_\_\_\_\_ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.  
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).  
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

### Priority under 35 U.S.C. § 119

- 12) ☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☒ All    b) ☐ Some \*    c) ☐ None of:
1. ☒ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

\* See the attached detailed Office action for a list of the certified copies not received.

### Attachment(s)

- |                                                                                      |                                                                   |
|--------------------------------------------------------------------------------------|-------------------------------------------------------------------|
| 1) <input checked="" type="checkbox"/> Notice of References Cited (PTO-892)          | 4) <input type="checkbox"/> Interview Summary (PTO-413)           |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | Paper No(s)/Mail Date. _____                                      |
| 3) <input type="checkbox"/> Information Disclosure Statement(s) (PTO/SB/08)          | 5) <input type="checkbox"/> Notice of Informal Patent Application |
| Paper No(s)/Mail Date _____                                                          | 6) <input type="checkbox"/> Other: _____                          |

### DETAILED ACTION

**Status of the claims:** Claims 1-31, 33, 35, 37-39, 41, 43-45, 47, 49-52, 58, 60-74 are currently pending.

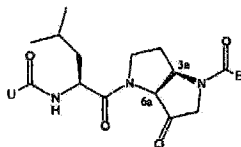
**Priority:** This application is a 371 of PCT/GB03/02957 (07/15/2003) which claims benefit of 60/418,524 (10/15/2002) and foreign priority to UNITED KINGDOM 0216525.6 (07/16/2002) and UNITED KINGDOM 0217239.3 (07/25/2002).

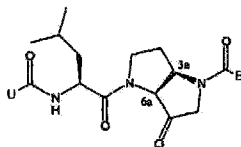
**IDS:** No IDS was filed with this application.

### *Election/Restrictions*

1. Applicant's election without traverse of Group I in the reply filed on 7/2/2008 is acknowledged. The groups were defined as follows in the requirement for restriction dated 1/2/2008:

Group I, claim(s) 1-31, 33, 35, 37-39, 41, 43-45, 47, 49-51, 58, 73, 74, in part, drawn to



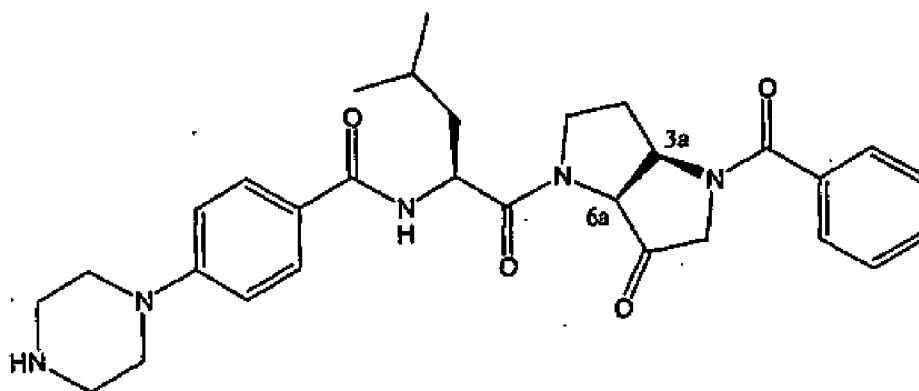
a product with the core formula , wherein B is phenyl. An election for search purposes is required with this group.

Group II, claim(s) 1-31, 33, 35, 37-39, 41, 43-45, 47, 49-51, 58, 73, 74, in part, drawn to a product not encompassed by Group I. An election for search purposes is required with this group. Election of this group may require further restriction.

The requirement is still deemed proper and is therefore made FINAL.

Applicant also elected the following species (allegedly reading on claims 1-8, 13-28, 30, 31, 49, 51, 58, 73 and 74):

**EXAMPLE 194. (3a*R*, 6a*S*)-*N*-[(1*S*)-1-(4-Benzoyl-6-oxo-hexahydro-pyrrolo[3,2-*b*] pyrrole-1-carbonyl)-3-methyl-butyl]-4-piperazin-1-yl-benzamide**



Because the generic claim was found unpatentable as detailed below, the claims are restricted to the elected species ONLY and the remaining subject matter held withdrawn. Therefore, claims 9-12, 29, 33, 35, 37-39, 41, 43-45, 47, 50, 52, 60-72 are withdrawn in their entirety and the subject matter outside of the elected species withdrawn from claims 1-8, 13-28, 30, 31, 49, 51, 58, 73 and 74.

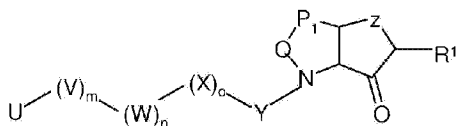
***Double Patenting***

2. The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. A nonstatutory obviousness-type double patenting rejection is appropriate where the conflicting claims are not identical, but at least one examined application claim is not patentably distinct from the reference claim(s) because the examined application claim is either anticipated by, or would have been obvious over, the reference claim(s). See, e.g., *In re Berg*, 140 F.3d 1428, 46 USPQ2d 1226 (Fed. Cir. 1998); *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) or 1.321(d) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent either is shown to be commonly owned with this application, or claims an invention made as a result of activities undertaken within the scope of a joint research agreement.

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

3. Claim 1 is rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claim 1 of copending Application Nos. 10/466384 and 12/072414. Although the conflicting claims are not identical, they are not patentably distinct from each other because the scope of the claims substantially overlap in the two applications, for example, '384 claims compounds of the formula



### ***Claim Rejections - 35 USC § 112***

4. The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

5. Claims 1-8, 13-28, 30, 31, 49, 58, 73 and 74 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly

connected, to make and/or use the invention. The claims while potentially being enabled for salts, hydrates, and solvates is not enabled for complexe or prodrug.

The factors to be considered in determining whether a disclosure meets the enablement requirements of 35 U.S.C. 112, first paragraph, have been described in *In re Wands*, 858 F.2d 731, 8 USPQ2d 1400 (Fed. Cir., 1988). The court in *Wands* states, "Enablement is not precluded by the necessity for some experimentation, such as routine screening. However, experimentation needed to practice the invention must not be undue experimentation. The key word is 'undue', not 'experimentation'" (*Wands*, 8 USPQ2d 1404). Clearly, enablement of a claimed invention cannot be predicated on the basis of quantity of experimentation required to make or use the invention. "Whether undue experimentation is needed is not a single, simple factual determination, but rather is a conclusion reached by weighing many factual considerations" (*Wands*, 8 USPQ2d 1404). Among these factors are: (1) the nature of the invention; (2) the breadth of the claims; (3) the state of the prior art; (4) the predictability or unpredictability of the art; (5) the relative skill of those in the art; (6) the amount of direction or guidance presented; (7) the presence or absence of working examples; and (8) the quantity of experimentation necessary.

While all of these factors are considered, a sufficient amount for a *prima facie* case is discussed below.

*(1) The nature of the invention and (2) the breadth of the claims:*

The claims are drawn to pharmaceutical compound complexe and prodrugs thereof with an unknown scope of what constitutes the complexing agent or prodrug derivative. Thus, the claims taken together with the specification imply an infinite number of possible complexes or prodrugs.

*(3) The state of the prior art and (4) the predictability or unpredictability of the art:*

Balant et al. teaches that prodrugs lacking adequate pharmacokinetic profiles require a large amount of experimentation and trial and error. Formation of complexes with pharmaceutical agents is highly unpredictable and often requires a detailed

correlation between structural elements and complex site before the formation would approach the level required to be predictable.

*(5) The relative skill of those in the art:*

Average.

*(6) The amount of direction or guidance presented and (7) the presence or absence of working examples:*

The specification does not provide any working examples or guidance as to the preparation of any particular prodrug or complex.

*(8) The quantity of experimentation necessary:*

Considering the state of the art as discussed by the references above, particularly with regards to making prodrugs and complexes and the high unpredictability in the art as evidenced therein, and the lack of guidance provided in the specification, one of ordinary skill in the art would be burdened with undue experimentation to practice the invention commensurate in the scope of the claims.

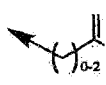
6. Claims 1-8, 13-28, 30, 31, 49, 58, 73 and 74 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. Each of the claims alternatively claim a "complex, or prodrug ... thereof" form of the compounds described. The specification defines the term prodrug as:

[0047] Prodrugs are any covalently bonded compounds which release the active parent drug according to general formula (I) in vivo.

which does not sufficiently convey to one skilled in the art what is being claimed. Also, the specification provides examples of what is meant by complexes, but a precise definition is given, leading to uncertainty for one of ordinary skill in the art as to what is actually claimed. Furthermore, nothing in the claims themselves or in the specification indicates that the inventors had possession of the claimed "prodrug" or "complex" form of the invention.

7. The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

8. Claim 1 is rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. One of ordinary skill in the art would find claim 1 to be incomprehensible and they would have to go to great lengths to determine whether any given compound was encompassed by the claim language, variables, provisos, etc.. Applicant should present the claims in a manner consistent with one of ordinary skill in the art's ability to read chemical formulae. The excessive use of variables (for example, A, B, D, G, E, K, J, L, M, R T, T<sub>2</sub>, T<sub>3</sub>, T<sub>4</sub>, T<sub>5</sub>, T<sub>6</sub>, Z, R<sup>1-22</sup>, Q, Y, U, V, W, X, Y, m, n, o, P<sub>1</sub>, P<sub>2</sub>, etc.), "=", "stable", , and provisos preclude reasonable interpretation of the claims.

***Claim Objections***



9. The pending claims are objected for reading on non-elected subject matter.
10. Claims 2-8, 13-28, 30, 31, 49, 58, 73 and 74 are objected to for being dependent on a rejected base claim.

### ***Specification Objections***

11. The title of the invention is not descriptive. A new title is required that is clearly indicative of the invention to which the claims are directed.

### ***Correspondence***

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Robert Havlin whose telephone number is (571) 272-9066. The examiner can normally be reached on Mon. - Fri., 7:30am-5pm EST.

If attempts to reach the examiner by telephone are unsuccessful the examiner's supervisor, Joe McKane can be reached at (571) 272-0699. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

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Art Unit 1626

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Primary Examiner, Art Unit 1626